APPENDIX F: Non-Technical Description of Experiment

Gaucher's disease is an inherited disease which causes a fatty substance to accumulate in bone marrow derived cells called macrophages. This accumulation of fat is due to the abnormality in an enzyme called glucocerebrosidase and results in many health problems. Currently, two forms of treatment are available. One consists of repeated intravenous injections of normal enzyme. This treatment needs to be continued life-long and is very expensive. The second form of treatment is transplantation of bone marrow from a suitable healthy donor. This treatment has a risk of transplant-related mortality. Furthermore, only about ¼ of the patients have a suitable marrow donor.

A possible new treatment is called gene therapy. A normal glucocerebrosidase gene is transferred into peripheral blood stem cells of a patient with Gaucher's disease. Stem cells are special cells which are able to produce platelets, red blood cells and white blood cells, including macrophages. The normal glucocerebrosidase gene is transferred into stem cells using modified viruses called retrovirus vectors which act as carriers of the gene. Once the gene is transferred into the stem cell, all the cells produced by the stem cell will contain the glucocerebrosidase gene, including the macrophages. This treatment, if successful, will provide the patient life-long with macrophages which contain a functioning glucocerebrosidase enzyme and are, therefore, not accumulating anymore fat and thereby causing disease. The retrovirus vectors used as carriers for the gene are altered such that they can transfer the gene to the stem cell but they cannot cause an infection.

Patients entered into this study will be treated for 4 days with a hormone-like drug called G-CSF, which increases the number of stem cells in the blood. On days 4 and 5 of G-CSF treatment, the patient's peripheral blood cells will be obtained by leukapheresis (peripheral blood cell collections with special machines). Cells will be enriched for stem cells using a device which selectively retains cells carrying the CD34 marker which is also on the surface of stem cells. The stem cell rich fraction will then be exposed to retrovirus vectors which transfer the glucocerebrosidase gene into the stem cells. The cells with the new gene will then be infused into the patient by injection into a blood vessel. This procedure of peripheral blood cell harvest, genetic alteration, and infusion into the patient will be repeated two more times at 2-month intervals. The patients will be observed for any possible side effect that may result from this treatment. Samples of blood and marrow cells will be obtained periodically and analyzed for the number of cells that contain the new gene and for the amount of glucocerebrosidase produced by these cells.